REMARKS

I. Status of the Claims

Claims 11-19 are pending in the application, claims 1-10 having been canceled previously. The claims stand rejected under 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §103

Claims 11-19 remain rejected as obvious over Chouini-Lalanne *et al.* in view of Ajmone-Cat *et al.* Chouini-Lalanne is cited as teaching supercoiled phage DNA, 10 mM NaCl, and one of four different NSAIDs. Ajmone-Cat is cited for teaching the popularity of NSAIDs and that flurbiprofen inhibits PGE_2 production. The examiner argues that it would have been obvious to determine the concentration of chloride ions and the concentration of NSAID in preparing a pharmaceutical. Applicants traverse.

The examiner has indicated that the limitation of pharmaceutical formulation may be properly ignored in interpreting the claims and applying the prior art. Applicants submit that this is not true – limitations must be considered on their merits. Whether a pharmaceutical formulation would be enough to establish patentability, once considered, is dependent on the facts of a particular case. Indeed, *In re Lerner*, 169 USPQ 51 (CCPA 1971) stands for the proposition that an otherwise unpatenable compound is not rendered patentable by addition of a carrier or diluent. However, if the use of the carrier would not be obvious, the resulting composition ***could*** be patentable. *In re Riden et al.*, 138 USPQ 112 (CCPA 1963); *Ex parte Billman*, 71 USPQ 253 (POBA 1946); *Ex parte Erdmann et al.*, 194 USPQ 96 (POBA 1975).

In response, the examiner continues to argue that "nothing about the phrase 'pharmaceutical formulation' implies that it can be only for in vivo use, and pharmaceutical drugs are routinely tested in vitro." This obfuscuted argument holds no merit. Applicants are their own lexicographers, and the examiner is ***compelled*** to interpret the claims and terms therein in light of applicants' specification. At page 7, lines 16-24, applicants provide a ***detailed*** explanation of the claim term in question:

> The term "formulation" or "pharmaceutical formulation" as used in the present document means the pharmaceutical form of preparation, for example, for a drug or an inoculation medium, which his administered *in vivo* to a human or an animal, or *in vitro* or *ex vivo* to organs, tissues or cells, consisting of one or more active ingredients and auxilliary formulation agents. Active ingredients according to the present invention are nucleic acids.

There would be little need, given this ***explicit*** definition of "pharmaceutical formulation" to proceed to an extrinsic source, but if that were done, a wholly consistent definition would be found:

> Pharmaceutical formulation, in pharmaceutics, is the process in which different chemical substances are combined to a pure drug substance to produce a final medicinal product.
>
> Formulation studies involve developing a preparation of the drug which is both stable and acceptable to the patient. For orally taken drugs, this usually involves incorporating the drug into a tablet or a capsule. It is important to appreciate that a tablet contains a variety of other substances apart from the drug itself, and studies have to be carried out to ensure that the drug is compatible with these other substances.

See www.answers.com. Thus, there is no question that this claim term clearly limits the subject matter to materials suitable for administration to subject *in vivo*.

In addition, the examiner argues that this does not exclude non-*in vivo* uses. This comment is completely irrelevant. Just because a composition of matter may be used in ways

that are not intended, it does ***not*** mean that the examiner is free to ignore limitations that relate to other uses. This rejection is one for ***obviousness***, not inherent anticipation, and thus the question is ***why*** one would modify the teachings of Chouini-Lalanne, which discloses the use of DNA as a ***target*** for possible phototoxic actions of NSAIDs, to prepare a formulation suitable not just for the *in vitro* test that was described, but for *in vivo* administration of a DNA-NSAID combination. As discussed previously, Ajmone-Cat cannot provide any such motivation given that it merely discusses NSAIDs, and thus says nothing about adding DNA to pharmaceutical formulation of an NSAID.

Once again, it is black letter law that the examiner ***must*** take into consideraton the pharmaceutical formulation limitation of the present claims, and when properly considered, it is clear that the cited prior art fails to suggest such an invnetion. This fact alone would establish the patentability of the rejected claims.

However, this is not the only limitation that the examiner must address. In addition, claim 1 differs from the teachings of Chouini-Lalanne at least by having a pH range of 6.2-7.0, as opposed to 7.4. There is no comparable disclosure of pH ranges in Ajmone-Cat, so the question is one of whether there is sufficient motivation to modify the pH range from 7.4 to at last 7.0. It is well-established that ***some*** motivation must be provided by the examiner - either in the prior art or in the general knowledge in the field. None is present here.

The examiner continues to argue that the present invention is mere "optimization," which is not patentable. However, applicants submit that even "optimization" requires some motivation, and looking at Chouini-Lalanne, the reference uses a pH 7.4 phosphate buffer to dilute DNA and NSAIDs, and the resulting reaction is performed in a test tube. What motivation is there to drop the pH from the stated 7.4 level to 6.2-7.0? Applicants submit that the answer is

none, and hand-waiving regarding optimiziation is insufficient, because you can only optimize that for which there is motivation to cause change. Ajmone-Cat is of no avail as it does not discuss using anything but NSAIDs, and so why both to "optimize" the composition of Chouini-Lalanne when no *in vivo* use for such is contemplated?

In a vain attempt to justify this line of reasoning, the examiner argues that there is still sufficient motivation from applicants intended *in vivo* use to drop the pH from Chouini-Lalanne's 7.4 "to the art accepted physiological neutral pH of 7.0" (emphasis in original). This approach is doubly objectionable. First, the examiner has denied there is any *in vivo* implications for the instant claims. Assuming that were proper, how would one of skill in the art, looking at applicants' claims, discern such *in vivo* intent? Thus, entire line of argument is unjustified. Second, and more critically, where is there evidence that physiological pH is 7.0? Indeed, a quick persual of the interet reveals that physiologic pH is 7.35-7.4 (see www.answers.yahoo.com; en.wiktionary.org), essentially that set forth by Chouini-Lalanne. Hence, again, ***there is no motivation to modify that reference to arrive at the claimed invention***. Applicants therefore call for an Examiner's Affidavit under 37 C.F.R. §1.104(d)(2) to support reliance on personal knowledge of PTO personnel. In the absence of such information, or a scientific citation to counter applicants' position, applicants' factual averments regarding physiologic pH must be admitted.

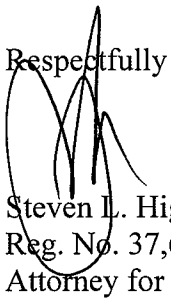
Finally, though not required, applicants again submit that even if there were a *prima facie* case of obviousness, the evidence or record shows a surprising result stemming from loweing of the pH from 7.4 to 7.0, namely, ***an increase in DNA uptake of 50%***. Thus, although no "special property" is required for patentability here, this clearly is one as the examiner has not denied that such an increase would indeed be surprising.

In sum, there is no legal basis for motivation to combine the cited art, even ***general*** motivation, nor is the presently claimed invention one of optimization, and even if it were, the surprising results of record would still render the claimed invention patentable over the cited art. Therefore, reconsideration and withdrawal of the rejection is therefore respectfully requested.

III. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding the content of this preliminary amendment, a telephone call to the undersigned is invited.

Respectfully submitted,



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